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NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS
RESEARCH LABORATORY
RESEARCH TRIANGLE PARK, NC 27711

SFUND RECORDS CTR
44933

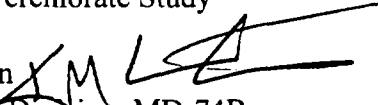
OFFICE OF
RESEARCH AND DEVELOPMENT

CROFTON, 1998h

MEMORANDUM

Date: 10 October 1998 (revised 28 October 1998)

Subject: Analysis and Graphics of Thyroid Hormone Data from the Rabbit
Developmental Perchlorate Study

From: Kevin M. Crofton 
Neurotoxicology Division, MD-74B
National Health Effects and Environmental Research Laboratory

To: Annie Jarabek
National Center for Environmental Assessment

Attached is the statistical analysis of the data from the Rabbit Developmental Study conducted by the Argus Research Laboratories (Argus #1416-002). I have attached a short description of how the analysis was done and some summary graphs. This memo supercedes my previous analysis memo of 10/10/98. This new analysis was needed after it was revealed that the original report did not separate pregnant from non-pregnant animals.

Note: The raw data used in this analysis is the same as that found in the report (Argus, 1998c) submitted to the Agency. This analysis also used the pregnancy status information recently submitted (York, 1998e).

Analyses of Thyroid Hormone and Thyrotrophin Data from the Argus Rabbit Developmental Perchlorate Study

Summary: The Argus report #1416-002 summarizes data from a developmental toxicity study of ammonium perchlorate in rabbits. This analysis contains data from both pregnant and non-pregnant rabbits. The analyses for non-pregnant animals is not useful due to the very limited number of subjects per group, therefore, the analyses for these two group were conducted separately. I conducted a statistical analysis of the thyroid and pituitary hormone data (T4, thyroxine; T3, triiodothyronine; TSH, thyroid stimulating hormone) found in that report. Results of these re-analyses are different from those stated in the report. The report states that the NOEL for T4 was 10 mg/kg/day. The current analysis, excluding non-pregnant animals, demonstrates a NOEL 0.1 mg/kg/day. There were statistically significant decreases in T4 at the 1, 10, 30 and 100 mg/kg/day group. There was no statistical significance of any dose on T3 or TSH.

Data: All data were taken from Appendix I from the Argus report. Data from dependent measures (T3, T4, TSH) were subjected to separate one-way ANOVAs, with Treatment (dose) as the independent between-subjects variable. Mean contrasts were performed using Tukey's Studentized Range (HSD) Test. To correct for multiple comparisons (i.e., three separate ANOVAs) the acceptable alpha for significance (for all interaction main effects tests) was corrected to 0.0289 (alpha of 0.05 divided by the square root of the number of dependent variables). SAS analysis code and output are attached.

Data Analysis - Results:

Total Serum Thyroxine (T4): There was a main effect of Treatment and a significant difference between group means for the control vs 1, 10, 30 and 100 mg/kg/day groups. These data are plotted in Figure 1.

Total Serum Triiodothyronine (T3): The main effect of Treatment was not significant for T3. Data are plotted in Figure 2.

Thyroid Stimulating Hormone (TSH): The main effect of Treatment was not significant for TSH. Data are plotted in Figure 3.

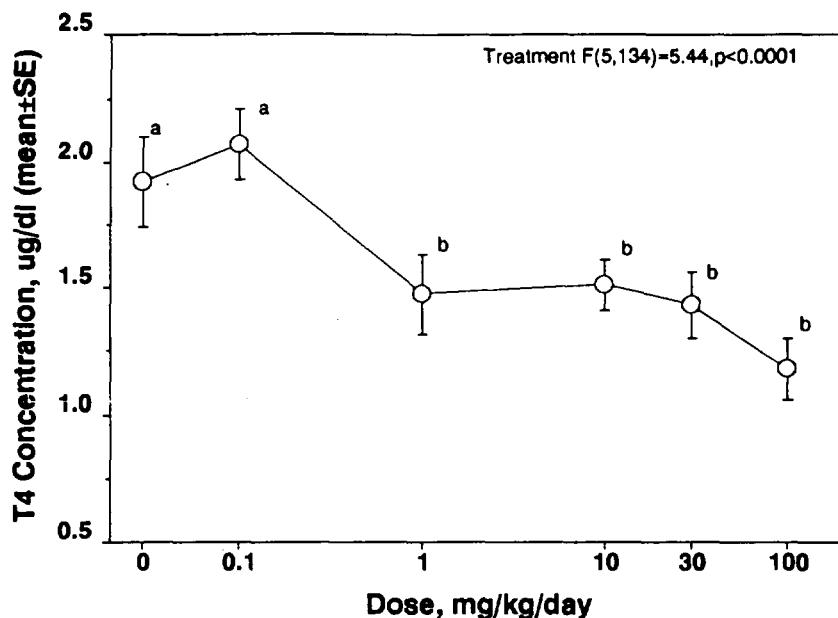


Figure 1. Effects of perchlorate exposure in pregnant rabbits. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was a main effects of Treatment. Means with different letters were significantly different ($p<0.05$, Tukey's after significant main effect). Daily dose was estimated from water consumption data.

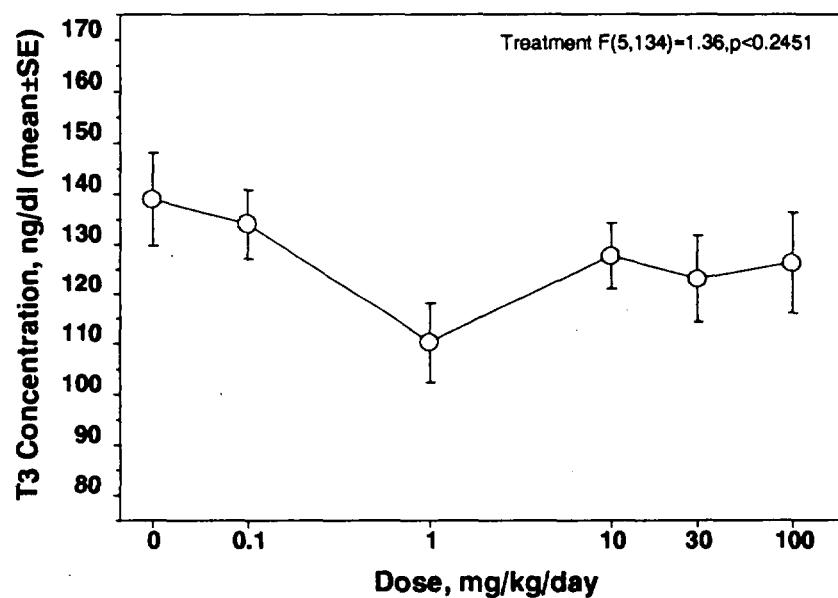


Figure 2. Lack of effects of perchlorate exposure in pregnant rabbits on T3. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was no significant effect of Treatment. Daily dose was estimated from water consumption data.

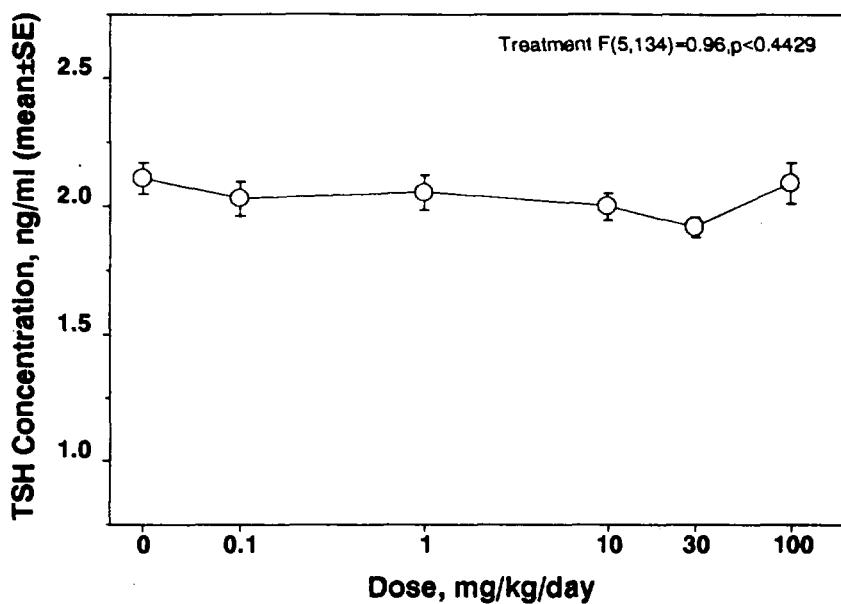


Figure 3. Lack of effects of perchlorate exposure in pregnant rabbits on TSH. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was no significant effect of Treatment. Daily dose was estimated from water consumption data.

Analyses of Thyroid Hormone and Thyrotrophin Data from the Argus Rabbit Developmental Perchlorate Study

Summary: The Argus report #1416-002 summarized data from a Developmental Toxicity Study of ammonium perchlorate in rabbits. This analysis contains data from both pregnant and non-pregnant rabbits. The analyses for non-pregnant animals is not useful due to the very limited number of subjects per group, therefore, the analyses for these two group were conducted separately. I conducted a statistical analysis of the thyroid and pituitary hormone data (T4, thyroxine; T3, triiodothyronine; TSH, thyroid stimulating hormone) found in that report. Results of these re-analyses are different from those stated in the report. The report states that the NOEL for T4 was 10 mg/kg/day. The current analysis, excluding non-pregnant animals, demonstrates a NOEL 0.1 mg/kg/day. There were statistically significant decreases in T4 at the 1, 10, 30 and 100 mg/kg/day group. There was no statistical significance of any dose on T3 or TSH.

Data: All data were taken from Appendix I from the Argus report. Data from dependent measures (T3, T4, TSH) were subjected to separate one-way ANOVAs, with Treatment (dose) as the independent between-subjects variable. Mean contrasts were performed using Tukey's Studentized Range (HSD) Test. To correct for multiple comparisons (i.e., three separate ANOVAs) the acceptable alpha for significance (for all interaction main effects tests) was corrected to 0.0289 (alpha of 0.05 divided by the square root of the number of dependent variables). SAS analysis code and output are attached.

Data Analysis - Results:

Total Serum Thyroxine (T4): There was a main effect of Treatment and a significant difference between group means for the control vs 1, 10, 30 and 100 mg/kg/day groups. These data are plotted in Figure 1.

Total Serum Triiodothyronine (T3): The main effect of Treatment was not significant for T3. Data are plotted in Figure 2.

Thyroid Stimulating Hormone (TSH): The main effect of Treatment was not significant for TSH. Data are plotted in Figure 3.

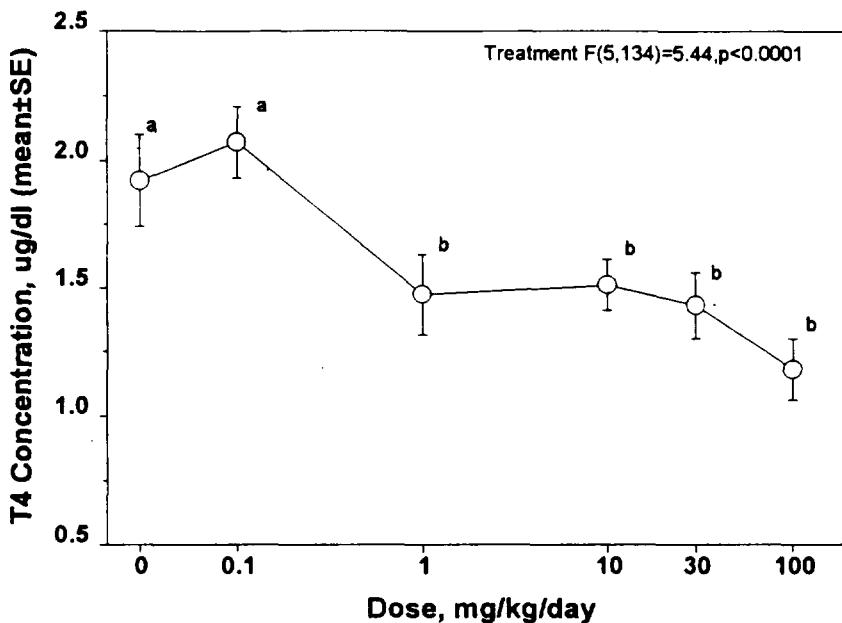


Figure 1. Effects of perchlorate exposure in pregnant rabbits. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was a main effects of Treatment. Means with different letters were significantly different ($p<0.05$, Tukey's after significant main effect). Daily dose was estimated from water consumption data.

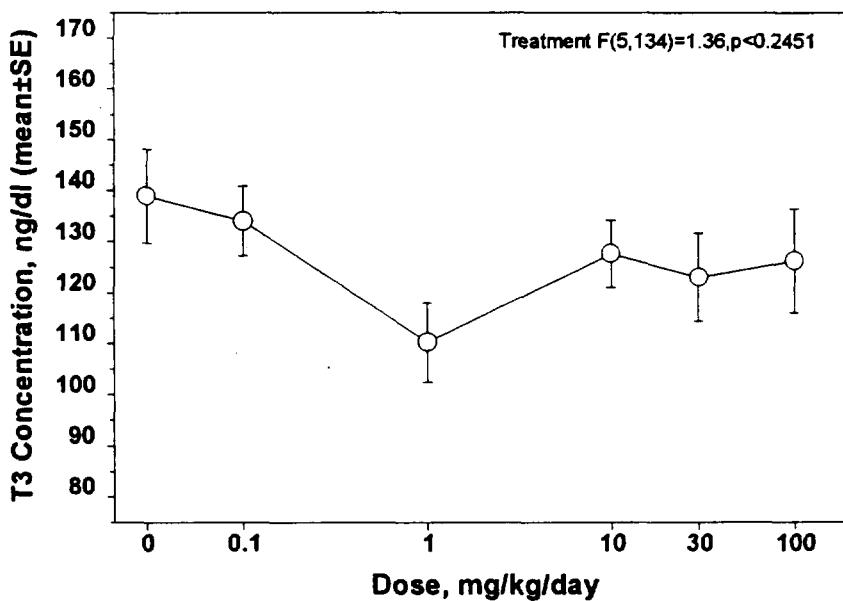


Figure 2. Lack of effects of perchlorate exposure in pregnant rabbits on T3. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was no significant effect of Treatment. Daily dose was estimated from water consumption data.

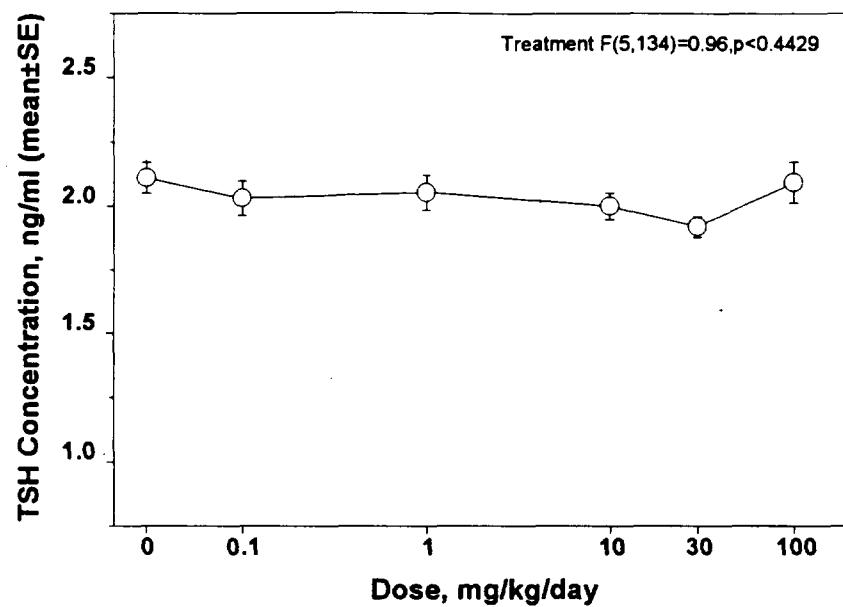


Figure 3. Lack of effects of perchlorate exposure in pregnant rabbits on TSH. Rabbits were exposed from days 6 to 28 of gestation. Samples were obtained on gestation day 28. There was no significant effect of Treatment. Daily dose was estimated from water consumption data.

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The SAS System

12:26

NOTE: Copyright © 1989-1996 by SAS Institute Inc., Cary, NC, USA.

NOTE: SAS (r) Proprietary Software Release 6.12 TS020

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NOTE: Running on ALPHASERVER Model 2100 5/300 Serial Number 80000000.

Welcome to the NHEERL-RTP SAS Information Delivery System.

```

1      *THIS FILE IS FOUND AT [CROFTON.THYROID.perchlorate]PERCHLORATE_RABBIT.SAS;
2      *IT ANALYZES THE THYROID HORMONE DATA FROM THE WPAFB 90 DAY PERCHLORATE STUDY;
3
4
5      *INPUT DATA INTO SAS DATASET;
6      DATA RAW; INFILE '[CROFTON.THYROID.PERCHLORATE]PERCHLORATE_RABBIT.TXT';
7          INPUT ANIM$ DOSE$ GENDER$ AGE$ PREGSTAT$ T3 T4 TSH CYST$ ECTOP$ 
8              IREGCYST$ MONONUC$ FOLHYPERS$ ATROPHY$;
9
10     * DEFINITIONS OF VARIABLE NAMES:
11     *      ANIM = ANIMAL ID#;
12     *      DOSE = TREATMENT CODE;
13     *      AGE = AGE IN DAYS OF GESTATION;
14     *      PREGSTAT = PREGNANCY STATUS, NP=NOT PREGNANT, P=PREGNANT;
15     *      T3 = TOTAL SERUM TRIIODOTHYRONINE, NG/DL;
16     *      T4 = TOTAL SERUM THYROXINE, NG/DL;
17     *      TSH = TOTAL SERUM THYROID STIMULATION HORMONE, NG/DL;
18     *      CYST = PRESENCE OF THYROID GLAND CYSTS;
19     *      ECTOP = PRESENCE OF ECTOPIC THYMIC TISSUE;
20     *      IREGCYST = RANK SCORE OF IRREGULAR/CYSTIC FOLLICLES;
21     *      MONONUC = RANK SCORE OF A FOCAL INFILTRATION OF MONONUCLEAR CELLS;
22     *      HYPER = RANK SCORE OF FOLLICULAR CELL HYPERTROPHY;
23     *      ATROPHY = RANK SCORE OF FOCAL EPITHELIAR ATROPHY;
24
25     *NOTES FOR DICHOTOMOUS VARIABLES:
26     *      * = NO PRESENT, SPECIFICALLY LISTED IN REPORT;
27     *      P = PRESENT, SPECIFICALLY LISTED IN REPORT;
28     *      N = NOT PRESENT, NOT LISTED IN REPORT;
29
30     *NOTES FOR RANKED SCORES;
31     *      INCIDENCE WAS RANKED FROM 1-4;
32     *      * = INCIDENCE ABSENT, SPECIFICALLY LISTED IN REPORT;
33     *      N = INCIDENCE ABSENT, NOT LISTED IN REPORT;
34
35
36     *ASSIGN TREATMENT VALUES TO DOSE CODES;
37     IF DOSE = '1' THEN TRT = '1-----Control';
38     IF DOSE = '2' THEN TRT = '2-0.1mg/kg/day';

```

```
39 IF DOSE = '3' THEN TRT = '3-1.0mg/kg/day';
40 IF DOSE = '4' THEN TRT = '4--10mg/kg/day';
41 IF DOSE = '5' THEN TRT = '5--30mg/kg/day';
42 IF DOSE = '6' THEN TRT = '6-100mg/kg/day';
43
44
```

NOTE: The infile '[CROFTON.THYROID.PERCHLORATE] PERCHLORATE_RABBIT.TXT' is:
File=DSA21:[SAS\$USERS.CROFTON.THYROID.PERCHLORATE] PERCHLORATE_RABBIT.TXT

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NOTE: 150 records were read from the infile '[CROFTON.THYROID.PERCHLORATE] PERCHLORATE_RABBIT.TXT'.
 The minimum record length was 143.
 The maximum record length was 143.
 NOTE: The data set WORK.RAW has 150 observations and 15 variables.

```
44      PROC PRINT;
45          TITLE "ORIGINAL RABBIT DEVELOPMENTAL DATA SET FOR ALL THYROID VARIABLES";
46
```

NOTE: The PROCEDURE PRINT printed pages 1-3.

```
47      DATA CONVERT; SET RAW;
48
49      *ASSIGN A VALUE OF 0 TO ALL MISSING OR '**' VALUES, ASSING A VALUE OF 1 TO ALL 'P' VALUES;
50      IF CYST = 'N' THEN CYST = '0';
51      IF CYST = '**' THEN CYST = '0';
52      IF CYST = 'P' THEN CYST = '1';
53
54      IF ECTOP = 'N' THEN ECTOP = '0';
55      IF ECTOP = '**' THEN ECTOP = '0';
56      IF ECTOP = 'P' THEN ECTOP = '1';
57
58      IF IREGCYST = 'N' THEN IREGCYST = '0';
59      IF IREGCYST = '**' THEN IREGCYST = '0';
60
61      IF MONONUC = 'N' THEN MONONUC = '0';
62      IF MONONUC = '**' THEN MONONUC = '0';
63
64      IF FOLHYPER = 'N' THEN FOLHYPER = '0';
65      IF FOLHYPER = '**' THEN FOLHYPER = '0';
66
67      IF ATROPHY = 'N' THEN ATROPHY = '0';
68      IF ATROPHY = '**' THEN ATROPHY = '0';
69
70
```

NOTE: The data set WORK.CONVERT has 150 observations and 15 variables.

```
70      PROC PRINT;
71          TITLE "RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR OUTPUT";
72
73      *OUTPUT THE DATASET TO AN TEMPORARY ASCII FILE;
```

NOTE: The PROCEDURE PRINT printed pages 4-6.

```
74      DATA OUTPUT1; SET CONVERT;
75          FILE '[CROFTON.THYROID.PERCHLORATE] TEMP.ASC';
```

```
76      PUT ANIM 1-4 TRT 6-19 PREGSTAT T3 T4 TSH CYST ECTOP IREGCYST MONONUC FOLHYPER ATROPHY;  
77  
78      *INPUT ASCII DATASET AS ALL NUMERIC VARIABLES;
```

NOTE: The file '[CROFTON.THYROID.PERCHLORATE]TEMP.ASC' is:
File=DSA21:[SAS\$USERS.CROFTON.THYROID.PERCHLORATE]TEMP.ASC

NOTE: 150 records were written to the file '[CROFTON.THYROID.PERCHLORATE]TEMP.ASC'.
The minimum record length was 38.
The maximum record length was 50.

NOTE: The data set WORK.OUTPUT1 has 150 observations and 15 variables.

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```
79      DATA FINAL1; INFILE '[CROFTON.THYROID.PERCHLORATE]TEMP.ASC';  
80          INPUT ANIM TRT$ 6-19 PREGSTAT$ T3 T4 TSH CYST ECTOP IREGCYST MONONUC FOLHYPER ATROPHY;  
81  
82
```

NOTE: The infile '[CROFTON.THYROID.PERCHLORATE]TEMP.ASC' is:
File=DSA21:[SAS\$USERS.CROFTON.THYROID.PERCHLORATE]TEMP.ASC

NOTE: 150 records were read from the infile '[CROFTON.THYROID.PERCHLORATE]TEMP.ASC'.
The minimum record length was 38.
The maximum record length was 50.

NOTE: The data set WORK.FINAL1 has 150 observations and 12 variables.
82 PROC SORT; BY PREGSTAT TRT;
83

NOTE: The data set WORK.FINAL1 has 150 observations and 12 variables.
83 PROC PRINT;

```
84          TITLE "RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR ANALYSES";  
85
```

```
86      *GENERATE GROUP MEANS TABLES - SORT BY TREATMENT;  
87
```

NOTE: The PROCEDURE PRINT printed pages 7-9.
87 PROC SORT; BY PREGSTAT TRT;
88

NOTE: Input data set is already sorted, no sorting done.
88 PROC MEANS N MEAN STDERR SUM MIN MAX STD VAR CV; BY PREGSTAT TRT;
89 VAR T3 T4 TSH CYST ECTOP IREGCYST MONONUC FOLHYPER ATROPHY;
90 TITLE 'RABBIT DEVELOPMENTAL DATA - GROUP MEANS BY TREATMENT';
91
92 *RUN ONEWAY ANOVAS - FOR T3 T4 AND TSH VARIABLES;
93

NOTE: The PROCEDURE MEANS printed pages 10-13.

93 PROC SORT; BY PREGSTAT TRT;
94

NOTE: Input data set is already sorted, no sorting done.

94 PROC GLM; BY PREGSTAT;
95 CLASSES TRT;
96 MODEL T3 T4 TSH = TRT;
97 MEANS TRT/DUNCAN LINE;
98 TITLE1 "RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA";
99 TITLE2 "PROC GLM WITH TUKEYS";
100
101
102 ENDSAS;

NOTE: The PROCEDURE GLM printed pages 14-27.

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The SAS System

12:26

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414

1 ORIGINAL RABBIT DEVELOPMENTAL DATA SET FOR ALL THYROID VARIABLES

1

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ORIGINAL RABBIT DEVELOPMENTAL DATA SET FOR ALL THYROID VARIABLES

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ORIGINAL RABBIT DEVELOPMENTAL DATA SET FOR ALL THYROID VARIABLES

3

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OBS ANIM DOSE GENDER AGE PREGSTAT T3 T4 TSH CYST ECTOP IREGCYST MONONUC FOLHYPER ATROPHY

135	7696	2	F	29D	P	159.22	2.77	2.06	P	N	N	N	N	N
2-0.1mg/kg/day														
136	7714	3	F	29D	P	131.88	2.78	2.00	P	N	N	N	N	N
3-1.0mg/kg/day														
137	7654	1	F	29D	P	179.26	2.80	1.90	P	*	N	N	N	N
1-----Control														
138	7673	1	F	29D	P	209.30	2.84	2.69	*	*	2	*	N	N
1-----Control														
139	7751	5	F	29D	P	88.03	2.94	1.97	*	N	*	N	2	N
5--30mg/kg/day														
140	7682	2	F	29D	P	126.67	2.97	1.85	*	N	N	N	N	N
2-0.1mg/kg/day														
141	7745	4	F	29D	P	180.07	2.97	1.68	P	N	N	N	1	N
4--10mg/kg/day														
142	7662	1	F	29D	P	213.18	2.99	2.55	*	N	N	N	N	N
1-----Control														
143	7665	1	F	29D	P	168.41	3.18	2.06	*	N	N	N	N	N
1-----Control														
144	7712	3	F	29D	P	209.82	3.19	2.36	*	N	N	N	N	N
3-1.0mg/kg/day														
145	7667	1	F	29D	P	180.64	3.51	2.39	P	N	N	N	N	N
1-----Control														
146	7699	2	F	29D	P	194.76	3.67	1.87	P	N	N	N	N	N
2-0.1mg/kg/day														
147	7684	2	F	29D	P	132.28	4.07	2.02	*	N	N	N	N	N
2-0.1mg/kg/day														
148	7721	3	F	29D	P	.	.	.	P	N	N	*	N	N
3-1.0mg/kg/day														
149	7776	6	F	29D	P	.	.	.	*	N	N	N	*	N
6-100mg/kg/day														
150	7724	3	F	29D	P	.	.	.	P	N	N	1	N	N
3-1.0mg/kg/day														

1
November 2, 1998 4

RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR OUTPUT

12:26 Monday,

RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR OUTPUT														12:26 Monday,				
November 2, 1998		5		OBS	ANIM	DOSE	GENDER	AGE	PREGSTAT	T3	T4	TSH	CYST	ECTOP	IREGCYST	MONONUC	FOLHYPER	ATROPHY
				TRT														
1-----Control		57	7659	1	F	29D	P		98.27	1.29	1.86	1	0	0	0	0	0	
5--30mg/kg/day		58	7758	5	F	29D	P		85.39	1.29	1.72	0	0	0	0	0	0	
2-0.1mg/kg/day		59	7680	2	F	29D	P		81.65	1.29	2.28	1	0	0	0	0	0	
4--10mg/kg/day		60	7732	4	F	29D	P		70.04	1.29	1.82	0	0	2	0	0	0	
5--30mg/kg/day		61	7774	5	F	29D	P		103.41	1.30	1.63	1	0	0	0	2	0	
3-1.0mg/kg/day		62	7711	3	F	29D	P		79.66	1.32	1.94	1	0	0	0	0	0	
5--30mg/kg/day		63	7762	5	F	29D	P		101.51	1.32	2.09	0	0	0	0	3	0	
6-100mg/kg/day		64	7784	6	F	29D	P		132.58	1.34	2.07	0	0	0	0	1	0	
6-100mg/kg/day		65	7800	6	F	29D	P		131.58	1.35	1.93	1	0	0	0	1	0	
1-----Control		66	7663	1	F	29D	P		169.24	1.36	2.31	1	0	0	0	0	0	
4--10mg/kg/day		67	7746	4	F	29D	P		123.60	1.40	1.58	1	0	0	0	0	0	
4--10mg/kg/day		68	7741	4	F	29D	P		148.19	1.41	2.25	1	0	0	0	0	0	

1 RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR OUTPUT 12:26 Monday,
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OBS ANIM DOSE GENDER AGE PREGSTAT T3 T4 TSH CYST ECTOP IREGCYST MONONUC FOLHYPER ATROPHY
 TRT
 113 7794 6 F 29D P 282.17 2.06 2.33 0 0 0 0 1 0
 6-100mg/kg/day

138	7673	1	F	29D	P	209.30	2.84	2.69	0	0	2	0	0	0
1-----Control														
139	7751	5	F	29D	P	88.03	2.94	1.97	0	0	0	0	2	0
5--30mg/kg/day														
140	7682	2	F	29D	P	126.67	2.97	1.85	0	0	0	0	0	0
2-0.1mg/kg/day														
141	7745	4	F	29D	P	180.07	2.97	1.68	1	0	0	0	1	0
4--10mg/kg/day														
142	7662	1	F	29D	P	213.18	2.99	2.55	0	0	0	0	0	0
1-----Control														
143	7665	1	F	29D	P	168.41	3.18	2.06	0	0	0	0	0	0
1-----Control														
144	7712	3	F	29D	P	209.82	3.19	2.36	0	0	0	0	0	0
3-1.0mg/kg/day														
145	7667	1	F	29D	P	180.64	3.51	2.39	1	0	0	0	0	0
1-----Control														
146	7699	2	F	29D	P	194.76	3.67	1.87	1	0	0	0	0	0
2-0.1mg/kg/day														
147	7684	2	F	29D	P	132.28	4.07	2.02	0	0	0	0	0	0
2-0.1mg/kg/day														
148	7721	3	F	29D	P	.	.	.	1	0	0	0	0	0
3-1.0mg/kg/day														
149	7776	6	F	29D	P	.	.	.	0	0	0	0	0	0
6-100mg/kg/day														
150	7724	3	F	29D	P	.	.	.	1	0	0	1	0	0
3-1.0mg/kg/day														

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RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR ANALYSES

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OBS POLHYPER	ANIM ATROPHY	TRT	PREGSTAT	T3	T4	TSH	CYST	ECTOP	IREGCYST	MONONUC
1 0	7660 0	1-----Control	NP	159.94	0.57	1.73	1	1	0	0
2 0	7671 0	1-----Control	NP	224.04	2.07	2.42	0	1	0	0
3 0	7653 0	1-----Control	NP	162.82	1.98	1.77	0	0	0	0
4 0	7700 0	2-0.1mg/kg/day	NP	179.83	2.29	1.69	1	0	0	0
5 0	7739 0	4--10mg/kg/day	NP	180.61	1.92	1.93	0	0	0	0
6 1	7771 0	5--30mg/kg/day	NP	143.17	1.01	1.38	1	0	0	0
7 0	7795 0	6-100mg/kg/day	NP	153.89	0.86	2.07	0	0	0	0
8 0	7672 0	1-----Control	P	67.03	0.51	1.47	0	0	0	0
9 0	7666 0	1-----Control	P	167.78	0.71	2.18	0	0	0	0
10 0	7675 0	1-----Control	P	66.92	0.95	1.76	0	0	0	1
11 0	7658 0	1-----Control	P	100.28	1.09	2.11	1	0	0	0
12 0	7657 0	1-----Control	P	102.26	1.16	1.75	0	0	0	0
13 0	7655 0	1-----Control	P	102.63	1.20	1.97	0	0	0	0
14 0	7659 0	1-----Control	P	98.27	1.29	1.86	1	0	0	0
15 0	7663 0	1-----Control	P	169.24	1.36	2.31	1	0	0	0
16 0	7652 0	1-----Control	P	90.04	1.41	1.87	1	0	0	0
17 0	7656 0	1-----Control	P	93.53	1.53	2.38	1	0	0	0
18 0	7674 0	1-----Control	P	161.62	1.73	2.09	1	0	0	0
19 0	7661 0	1-----Control	P	146.27	2.10	2.21	0	0	0	0
20 0	7669 0	1-----Control	P	151.43	2.15	2.19	1	0	0	0
21 0	7651 0	1-----Control	P	118.56	2.16	2.77	0	0	0	0

22 0	7670 0	1-----Control	P	139.91	2.26	1.74	0	0	0	0
23 0	7664 0	1-----Control	P	164.10	2.59	2.20	0	0	0	0
24 0	7668 0	1-----Control	P	165.72	2.70	2.03	0	0	0	0
25 0	7654 0	1-----Control	P	179.26	2.80	1.90	1	0	0	0
26 0	7673 0	1-----Control	P	209.30	2.84	2.69	0	0	2	0
27 0	7662 0	1-----Control	P	213.18	2.99	2.55	0	0	0	0
28 0	7665 0	1-----Control	P	168.41	3.18	2.06	0	0	0	0
29 0	7667 0	1-----Control	P	180.64	3.51	2.39	1	0	0	0
30 0	7693 0	2-0.1mg/kg/day	P	154.84	1.07	1.92	0	0	0	0
31 0	7697 0	2-0.1mg/kg/day	P	127.35	1.21	1.97	1	0	0	0
32 0	7680 0	2-0.1mg/kg/day	P	81.65	1.29	2.28	1	0	0	0
33 0	7688 0	2-0.1mg/kg/day	P	113.81	1.43	1.76	1	0	0	0
34 0	7677 0	2-0.1mg/kg/day	P	84.52	1.59	1.64	1	0	0	0
35 0	7695 0	2-0.1mg/kg/day	P	206.18	1.60	1.97	0	0	0	0
36 0	7679 0	2-0.1mg/kg/day	P	77.74	1.61	2.57	0	0	0	0
37 0	7681 0	2-0.1mg/kg/day	P	132.04	1.80	1.76	0	0	0	0
38 0	7691 0	2-0.1mg/kg/day	P	119.67	1.88	2.13	0	0	0	0
39 0	7689 0	2-0.1mg/kg/day	P	151.32	1.92	2.01	1	0	0	0
40 0	7686 0	2-0.1mg/kg/day	P	108.50	1.92	1.90	0	0	0	0
41 0	7676 0	2-0.1mg/kg/day	P	125.12	1.93	1.52	0	0	0	0
42 0	7692 0	2-0.1mg/kg/day	P	136.06	1.97	3.06	1	0	0	0
43 0	7678 0	2-0.1mg/kg/day	P	146.34	2.00	2.25	0	0	0	0
44 0	7687 0	2-0.1mg/kg/day	P	112.87	2.04	2.06	0	0	0	0
45 0	7683 0	2-0.1mg/kg/day	P	101.12	2.04	1.58	1	0	0	0

46 0	7694 0	2-0.1mg/kg/day	P	135.92	2.08	2.34	0	0	0	0
47 0	7690 0	2-0.1mg/kg/day	P	164.27	2.11	2.42	0	0	0	0
48 0	7698 0	2-0.1mg/kg/day	P	196.72	2.35	1.89	1	0	0	0
49 0	7685 0	2-0.1mg/kg/day	P	134.39	2.41	2.03	1	0	0	0
50 0	7696 0	2-0.1mg/kg/day	P	159.22	2.77	2.06	1	0	0	0
51 0	7682 0	2-0.1mg/kg/day	P	126.67	2.97	1.85	0	0	0	0
52 0	7699 0	2-0.1mg/kg/day	P	194.76	3.67	1.87	1	0	0	0
53 0	7684 0	2-0.1mg/kg/day	P	132.28	4.07	2.02	0	0	0	0
54 0	7716 0	3-1.0mg/kg/day	P	131.20	0.49	1.98	1	0	0	0
55 0	7705 0	3-1.0mg/kg/day	P	69.45	0.57	2.19	0	0	0	0

RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR ANALYSES

1	8									12:26
Monday, November 2, 1998										
OBS	ANIM	TRT	PREGSTAT	T3	T4	TSH	CYST	ECTOP	IREGCYST	MONONUC
FOLHYPER	ATROPHY									
56 0	7725 0	3-1.0mg/kg/day	P	122.56	0.73	1.58	1	0	0	0
57 0	7704 0	3-1.0mg/kg/day	P	119.09	0.78	1.82	0	0	0	0
58 0	7702 0	3-1.0mg/kg/day	P	99.31	0.81	1.90	0	0	4	0
59 0	7706 0	3-1.0mg/kg/day	P	70.74	0.94	1.78	0	0	0	0
60 0	7701 0	3-1.0mg/kg/day	P	72.61	0.95	1.81	1	0	0	0
61 0	7719 0	3-1.0mg/kg/day	P	79.64	0.96	1.69	1	0	0	0
62 0	7708 0	3-1.0mg/kg/day	P	65.66	0.98	2.38	0	0	0	0
63 0	7703 0	3-1.0mg/kg/day	P	104.72	1.04	1.88	0	0	0	0
64 0	7722 0	3-1.0mg/kg/day	P	104.53	1.07	2.91	0	0	0	0
65 0	7709 0	3-1.0mg/kg/day	P	179.52	1.11	2.59	1	0	0	0
66 0	7711 0	3-1.0mg/kg/day	P	79.66	1.32	1.94	1	0	0	0

Day	Subject ID	Dose	Route	Mean AUC	Mean Cmax	SD AUC	SD Cmax	N	0	0	0
0	7723	3-1.0mg/kg/day	P	80.41	1.62	1.82	0	0	0	0	0
0	7720	3-1.0mg/kg/day	P	149.96	1.76	1.79	0	0	0	0	0
0	7715	3-1.0mg/kg/day	P	153.06	1.80	1.89	1	0	0	0	0
0	7718	3-1.0mg/kg/day	P	114.24	1.92	2.34	1	0	0	0	0
0	7707	3-1.0mg/kg/day	P	80.83	2.16	1.85	1	0	0	0	0
0	7717	3-1.0mg/kg/day	P	123.82	2.21	2.18	1	0	0	0	0
0	7710	3-1.0mg/kg/day	P	81.95	2.30	2.44	1	0	0	0	0
0	7713	3-1.0mg/kg/day	P	110.12	2.39	2.09	0	0	0	0	0
0	7714	3-1.0mg/kg/day	P	131.88	2.78	2.00	1	0	0	0	0
0	7712	3-1.0mg/kg/day	P	209.82	3.19	2.36	0	0	0	0	0
0	7721	3-1.0mg/kg/day	P	.	.	.	1	0	0	0	0
0	7724	3-1.0mg/kg/day	P	.	.	.	1	0	0	0	1
0	7750	4--10mg/kg/day	P	108.74	0.64	2.03	0	0	0	0	0
0	7736	4--10mg/kg/day	P	142.11	0.66	1.84	1	0	0	0	0
0	7735	4--10mg/kg/day	P	112.65	0.82	1.71	1	0	1	0	0
0	7727	4--10mg/kg/day	P	99.79	1.14	1.94	0	0	0	0	0
0	7726	4--10mg/kg/day	P	117.54	1.21	2.30	0	0	0	0	0
2	7743	4--10mg/kg/day	P	148.57	1.26	1.96	1	0	0	0	0
0	7732	4--10mg/kg/day	P	70.04	1.29	1.82	0	0	2	0	0
0	7746	4--10mg/kg/day	P	123.60	1.40	1.58	1	0	0	0	0
0	7741	4--10mg/kg/day	P	148.19	1.41	2.25	1	0	0	0	0
0	7744	4--10mg/kg/day	P	116.80	1.41	2.18	1	0	0	0	0
0	7729	4--10mg/kg/day	P	92.91	1.44	1.70	1	0	0	0	0
0	7749	4--10mg/kg/day	P	97.66	1.48	2.08	1	0	0	0	0

RABBIT DEVELOPMENTAL DATA SET - FINAL DATA SET FOR ANALYSES

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12:26

Monday, November 2, 1998

OBS ANIM TRT PREGSTAT T3 T4 TSH CYST ECTOP IREGCYST MONONUC
FOLHYPER ATROPHY

111	7752	5--30mg/kg/day	P	133.18	1.17	2.07	0	0	2	0
0	0	5--30mg/kg/day	P	106.10	1.25	2.35	1	0	0	0
112	7757	5--30mg/kg/day	P	88.68	1.26	1.89	0	0	0	0
3	0	5--30mg/kg/day	P	207.03	1.27	2.09	1	1	0	0
113	7773	5--30mg/kg/day	P	109.81	1.27	1.48	1	0	0	0
1	0	5--30mg/kg/day	P	85.39	1.29	1.72	0	0	0	0
114	7766	5--30mg/kg/day	P	103.41	1.30	1.63	1	0	0	0
2	0	5--30mg/kg/day	P	101.51	1.32	2.09	0	0	0	0
115	7755	5--30mg/kg/day	P	91.79	1.52	1.91	0	0	0	0
0	0	5--30mg/kg/day	P	134.48	1.57	1.81	0	0	0	0
116	7758	5--30mg/kg/day	P	145.38	2.21	1.77	0	0	2	0
0	0	5--30mg/kg/day	P	211.19	2.23	1.73	1	0	0	0
117	7774	5--30mg/kg/day	P	205.05	2.33	2.05	1	0	0	0
2	0	5--30mg/kg/day	P	196.22	2.35	2.01	0	0	0	0
118	7762	5--30mg/kg/day	P	152.59	2.59	1.85	1	0	0	0
3	0	5--30mg/kg/day	P	88.03	2.94	1.97	0	0	0	0
119	7756	5--30mg/kg/day	P	79.97	0.18	2.07	0	0	0	0
0	0	5--30mg/kg/day	P	76.12	0.25	1.70	1	0	0	0
120	7765	5--30mg/kg/day	P	82.93	0.27	3.21	1	0	0	0
0	0	5--30mg/kg/day	P	132.61	0.56	3.11	1	0	0	0
121	7761	5--30mg/kg/day	P	117.10	0.60	1.77	1	0	0	0
0	0	5--30mg/kg/day	P	64.88	0.66	1.84	1	0	0	0
122	7770	5--30mg/kg/day	P	78.30	0.70	2.18	1	0	0	0
0	0	5--30mg/kg/day	P	99.82	0.77	2.01	1	0	0	0
123	7768	5--30mg/kg/day	P	0	0	0	0	0	0	0
3	0	5--30mg/kg/day	P	0	0	0	0	0	0	0
124	7767	5--30mg/kg/day	P	0	0	0	0	0	0	0
3	0	5--30mg/kg/day	P	0	0	0	0	0	0	0
125	7760	5--30mg/kg/day	P	0	0	0	0	0	0	0
0	0	5--30mg/kg/day	P	0	0	0	0	0	0	0
126	7751	5--30mg/kg/day	P	0	0	0	0	0	0	0
2	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
127	7797	6-100mg/kg/day	P	0	0	0	0	0	0	0
3	3	6-100mg/kg/day	P	0	0	0	0	0	0	0
128	7777	6-100mg/kg/day	P	0	0	0	0	0	0	0
1	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
129	7785	6-100mg/kg/day	P	0	0	0	0	0	0	0
3	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
130	7791	6-100mg/kg/day	P	0	0	0	0	0	0	0
3	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
131	7796	6-100mg/kg/day	P	0	0	0	0	0	0	0
2	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
132	7788	6-100mg/kg/day	P	0	0	0	0	0	0	0
0	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
133	7778	6-100mg/kg/day	P	0	0	0	0	0	0	0
2	0	6-100mg/kg/day	P	0	0	0	0	0	0	0
134	7798	6-100mg/kg/day	P	0	0	0	0	0	0	0

0	135	7779	6-100mg/kg/day	P	123.56	0.88	1.86	1	0
0	136	7790	6-100mg/kg/day	P	111.29	1.15	2.11	1	0
1	137	7784	6-100mg/kg/day	P	132.58	1.34	2.07	0	0
1	138	7800	6-100mg/kg/day	P	131.58	1.35	1.93	1	0
1	139	7787	6-100mg/kg/day	P	146.54	1.42	2.03	0	0
1	140	7786	6-100mg/kg/day	P	75.24	1.47	2.14	0	0
3	141	7781	6-100mg/kg/day	P	100.98	1.48	1.66	0	0
0	142	7789	6-100mg/kg/day	P	179.77	1.58	2.17	0	0
0	143	7799	6-100mg/kg/day	P	117.44	1.61	1.66	0	0
1	144	7793	6-100mg/kg/day	P	190.48	1.62	1.74	0	0
1	145	7783	6-100mg/kg/day	P	77.51	1.63	1.87	0	0
0	146	7792	6-100mg/kg/day	P	186.46	1.77	2.37	1	0
0	147	7782	6-100mg/kg/day	P	151.90	1.88	2.06	0	0
1	148	7780	6-100mg/kg/day	P	165.22	1.97	2.25	1	0
0	149	7794	6-100mg/kg/day	P	282.17	2.06	2.33	0	0
1	150	7776	6-100mg/kg/day	P	.	.	.	0	0

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RABBIT DEVELOPMENTAL DATA - GROUP MEANS BY TREATMENT

12:26 Monday,

----- PREGSTAT=NP TRT=1 ----- Control

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	3	182.2666667	20.9032066	546.8000000	159.9400000	224.0400000	36.2054158
1310.83	19.8639809						
T4	3	1.5400000	0.4856954	4.6200000	0.5700000	2.0700000	0.8412491
0.7077000	54.6265631						
TSH	3	1.9733333	0.2236316	5.9200000	1.7300000	2.4200000	0.3873414
0.1500333	19.6287854						
CYST	3	0.3333333	0.3333333	1.0000000	0	1.0000000	0.5773503
0.3333333	173.2050808						
ECTOP	3	0.6666667	0.3333333	2.0000000	0	1.0000000	0.5773503
0.3333333	86.6025404						
IREGCYST	3	0	0	0	0	0	0
0							
MONONUC	3	0	0	0	0	0	0
0							
FOLHYPER	3	0	0	0	0	0	0
0							
ATROPHY	3	0	0	0	0	0	0
0							

----- PREGSTAT=NP TRT=2 - 0.1mg/kg/day -----

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	1	179.8300000	.	179.8300000	179.8300000	179.8300000	.
T4	1	2.2900000	.	2.2900000	2.2900000	2.2900000	.

TSH	1	1.6900000	.	1.6900000	1.6900000	1.6900000	.
CYST	1	1.0000000	.	1.0000000	1.0000000	1.0000000	.
ECTOP	1	0	.	0	0	0	.
IREGCYST	1	0	.	0	0	0	.
MONONUC	1	0	.	0	0	0	.
FOLHYPER	1	0	.	0	0	0	.
ATROPHY	1	0	.	0	0	0	.

PREGSTAT=NP TRT=4--10mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	1	180.6100000	.	180.6100000	180.6100000	180.6100000	.
T4	1	1.9200000	.	1.9200000	1.9200000	1.9200000	.
TSH	1	1.9300000	.	1.9300000	1.9300000	1.9300000	.
CYST	1	0	.	0	0	0	.
ECTOP	1	0	.	0	0	0	.
IREGCYST	1	0	.	0	0	0	.
MONONUC	1	0	.	0	0	0	.
FOLHYPER	1	0	.	0	0	0	.
ATROPHY	1	0	.	0	0	0	.

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RABBIT DEVELOPMENTAL DATA - GROUP MEANS BY TREATMENT

12:26 Monday,

----- PREGSTAT=NP TRT=5--30mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	1	143.1700000	.	143.1700000	143.1700000	143.1700000	.
T4	1	1.0100000	.	1.0100000	1.0100000	1.0100000	.
TSH	1	1.3800000	.	1.3800000	1.3800000	1.3800000	.
CYST	1	1.0000000	.	1.0000000	1.0000000	1.0000000	.
ECTOP	1	0	.	0	0	0	.
IREGCYST	1	0	.	0	0	0	.
MONONUC	1	0	.	0	0	0	.
FOLHYPER	1	1.0000000	.	1.0000000	1.0000000	1.0000000	.
ATROPHY	1	0	.	0	0	0	.

----- PREGSTAT=NP TRT=6-100mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	1	153.8900000	.	153.8900000	153.8900000	153.8900000	.
T4	1	0.8600000	.	0.8600000	0.8600000	0.8600000	.

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RABBIT DEVELOPMENTAL DATA - GROUP MEANS BY TREATMENT

12:26 Monday,

----- PREGSTAT=P TRT=2-0.1mg/kg/day

Variable Variance	N	CV	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
T3 1156.90	24	134.3066667	6.9429130	3223.36	77.7400000	206.1800000	34.0131886	
	25.3250188							
T4 0.5072346	24	2.0720833	0.1453780	49.7300000	1.0700000	4.0700000	0.7122040	
	34.3713997							
TSH 0.1129297	24	2.0358333	0.0685960	48.8600000	1.5200000	3.0600000	0.3360502	
	16.5067619							
CYST 0.2590580	24	0.4583333	0.1038946	11.0000000	0	1.0000000	0.5089774	
	111.0496097							
ECTOP 0	24	0	0	0	0	0	0	0
IREGCYST 0	24	0	0	0	0	0	0	0
MONONUC 0	24	0	0	0	0	0	0	0
FOLHYPER 0	24	0	0	0	0	0	0	0
ATROPHY 0	24	0	0	0	0	0	0	0

----- PREGSTAT=P TRT=3-1.0mg/kg/day

Variable Variance	N	CV	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
T3 1395.54	23	110.2078261	7.7894543	2534.78	65.6600000	209.8200000	37.3569106	
	33.8967857							
T4 0.5649767	23	1.4730435	0.1567297	33.8800000	0.4900000	3.1900000	0.7516493	
	51.0269600							

TSH	23	2.0526087	0.0674382	47.2100000	1.5800000	2.9100000	0.3234223
0.1046020		15.7566461					
CYST	25	0.5600000	0.1013246	14.0000000	0	1.0000000	0.5066228
0.2566667		90.4683581					
ECTOP	25	0	0	0	0	0	0
0							
IREGCYST	25	0.1600000	0.1600000	4.0000000	0	4.0000000	0.8000000
0.6400000		500.0000000					
MONONUC	25	0.0400000	0.0400000	1.0000000	0	1.0000000	0.2000000
0.0400000		500.0000000					
FOLHYPER	25	0	0	0	0	0	0
0							
ATROPHY	25	0	0	0	0	0	0
0							

PREGSTAT=P TRT=4--10mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	24	127.6129167	6.6468095	3062.71	70.0400000	200.9300000	32.5625832
1060.32		25.5166828					
T4	24	1.5179167	0.1027678	36.4300000	0.6400000	2.9700000	0.5034574
0.2534694		33.1676594					
TSH	24	2.0025000	0.0528988	48.0600000	1.5800000	2.5200000	0.2591499
0.0671587		12.9413208					
CYST	24	0.6666667	0.0982946	16.0000000	0	1.0000000	0.4815434
0.2318841		72.2315119					
ECTOP	24	0	0	0	0	0	0
0							
IREGCYST	24	0.1250000	0.0915348	3.0000000	0	2.0000000	0.4484272
0.2010870		358.7417625					
MONONUC	24	0	0	0	0	0	0
0							
FOLHYPER	24	0.3750000	0.1451199	9.0000000	0	2.0000000	0.7109394
0.5054348		189.5838310					
ATROPHY	24	0	0	0	0	0	0
0							

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RABBIT DEVELOPMENTAL DATA - GROUP MEANS BY TREATMENT

12:26 Monday,

----- PREGSTAT=P TRT=5--30mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	24	123.8858333	8.7380953	2973.26	71.7500000	211.1900000	42.8077498
1832.50	34.5541929						
T4	24	1.4350000	0.1352534	34.4400000	0.4400000	2.9400000	0.6626036
0.4390435	46.1744641						
TSH	24	1.9379167	0.0422466	46.5100000	1.4800000	2.3500000	0.2069652
0.0428346	10.6797790						
CYST	24	0.4583333	0.1038946	11.0000000	0	1.0000000	0.5089774
0.2590580	111.0496097						
ECTOP	24	0.0416667	0.0416667	1.0000000	0	1.0000000	0.2041241
0.0416667	489.8979486						
IREGCYST	24	0.2500000	0.1379193	6.0000000	0	2.0000000	0.6756639
0.4565217	270.2655699						
MONONUC	24	0	0	0	0	0	0
0							
FOLHYPER	24	1.0000000	0.2481818	24.0000000	0	3.0000000	1.2158375
1.4782609	121.5837518						
ATROPHY	24	0	0	0	0	0	0
0							

----- PREGSTAT=P TRT=6-100mg/kg/day

Variable Variance	N	Mean	Std Error	Sum	Minimum	Maximum	Std Dev
		CV					
T3	23	126.2804348	10.6068259	2904.45	64.8800000	282.1700000	50.8685500
2587.61	40.2822100						
T4	23	1.1826087	0.1212358	27.2000000	0.1800000	2.0600000	0.5814263
0.3380565	49.1647224						

TSH	23	2.0930435	0.0822304	48.1400000	1.6600000	3.2100000	0.3943629
0.1555221	18.8416032						
CYST	24	0.5000000	0.1042572	12.0000000	0	1.0000000	0.5107539
0.2608696	102.1507837						
ECTOP	24	0	0	0	0	0	0
0							
IREGCYST	24	0	0	0	0	0	0
0							
MONONUC	24	0	0	0	0	0	0
0							
FOLHYPER	24	1.0833333	0.2163320	26.0000000	0	3.0000000	1.0598058
1.1231884	97.8282308						
ATROPHY	24	0.1250000	0.1250000	3.0000000	0	3.0000000	0.6123724
0.3750000	489.8979486						

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RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure
Class Level Information

Class Levels Values

TRT 5 1-----Control 2-0.1mg/kg/day 4--10mg/kg/day 5--30mg/kg/day 6-100mg/kg/day

Number of observations in by group = 7

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November 2, 1998 15

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Dependent Variable: T3

	Source	DF	Sum of Squares	Mean Square	F Value
Pr > F					
0.8552	Model	4	1610.78247619	402.69561905	0.31
	Error	2	2621.66426667	1310.83213333	
	Corrected Total	6	4232.44674286		
T3 Mean		R-Square	C.V.	Root MSE	
172.04285714		0.380580	21.04442	36.20541580	

	Source	DF	Type I SS	Mean Square	F Value
Pr > F					
0.8552	TRT	4	1610.78247619	402.69561905	0.31
Pr > F	Source	DF	Type III SS	Mean Square	F Value
0.8552	TRT	4	1610.78247619	402.69561905	0.31

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RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Dependent Variable: T4

Pr > F	Source	DF	Sum of Squares	Mean Square	F Value
0.7441	Model	4	1.44928571	0.36232143	0.51
	Error	2	1.41540000	0.70770000	
	Corrected Total	6	2.86468571		
T4 Mean	R-Square		C.V.	Root MSE	
1.52857143	0.505914		55.03499	0.84124907	

Pr > F	Source	DF	Type I SS	Mean Square	F Value
0.7441	TRT	4	1.44928571	0.36232143	0.51
Pr > F	Source	DF	Type III SS	Mean Square	F Value
0.7441	TRT	4	1.44928571	0.36232143	0.51

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November 2, 1998 17

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Dependent Variable: TSH

Source	DF	Sum of Squares	Mean Square	F Value
Pr > F				
Model	4	0.34670476	0.08667619	0.58
0.7126				
Error	2	0.30006667	0.15003333	
Corrected Total	6	0.64677143		
TSH Mean	R-Square	C.V.	Root MSE	
1.85571429	0.536055	20.87290	0.38734137	

Source	DF	Type I SS	Mean Square	F Value
Pr > F				
TRT	4	0.34670476	0.08667619	0.58
0.7126				
Source	DF	Type III SS	Mean Square	F Value
Pr > F				
TRT	4	0.34670476	0.08667619	0.58
0.7126				

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November 2, 1998 18

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Duncan's Multiple Range Test for variable: T3

NOTE: This test controls the type I comparisonwise error rate, not the
experimentwise error rate

Alpha= 0.05 df= 2 MSE= 1310.832

WARNING: Cell sizes are not equal.

Harmonic Mean of cell sizes= 1.153846

Number of Means	2	3	4	5
Critical Range	205.1	205.1	205.1	205.1

Means with the same letter are not significantly different.

Duncan Grouping	Mean	N	TRT
A	182.27	3	1-----Control
A	180.61	1	4--10mg/kg/day
A	179.83	1	2-0.1mg/kg/day
A	153.89	1	6-100mg/kg/day
A	143.17	1	5--30mg/kg/day

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November 2, 1998 19

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Duncan's Multiple Range Test for variable: T4

NOTE: This test controls the type I comparisonwise error rate, not the experimentwise error rate

Alpha= 0.05 df= 2 MSE= 0.7077

WARNING: Cell sizes are not equal.

Harmonic Mean of cell sizes= 1.153846

Number of Means	2	3	4	5
Critical Range	4.765	4.765	4.765	4.765

Means with the same letter are not significantly different.

Duncan Grouping	Mean	N	TRT
A	2.290	1	2-0.1mg/kg/day
A	1.920	1	4--10mg/kg/day
A	1.540	3	1-----Control
A	1.010	1	5--30mg/kg/day
A	0.860	1	6-100mg/kg/day

1
November 2, 1998 20

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=NP

General Linear Models Procedure

Duncan's Multiple Range Test for variable: TSH

NOTE: This test controls the type I comparisonwise error rate, not the
experimentwise error rate

Alpha= 0.05 df= 2 MSE= 0.150033
WARNING: Cell sizes are not equal.
Harmonic Mean of cell sizes= 1.153846

Number of Means 2 3 4 5
Critical Range 2.194 2.194 2.194 2.194

Means with the same letter are not significantly different.

Duncan Grouping	Mean	N	TRT
A	2.0700	1	6-100mg/kg/day
A			
A	1.9733	3	1-----Control
A			
A	1.9300	1	4--10mg/kg/day
A			
A	1.6900	1	2-0.1mg/kg/day
A			
A	1.3800	1	5--30mg/kg/day

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November 2, 1998 21

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

----- PREGSTAT=P
-----General Linear Models Procedure
Class Level Information

Class	Levels	Values
TRT	6	1-----Control 2-0.1mg/kg/day 3-1.0mg/kg/day 4--10mg/kg/day 5--30mg/kg/day 6-100mg/kg/day

Number of observations in by group = 143

NOTE: All dependent variable are consistent with respect to the presence or absence of missing values. However only 140 observations can be used in this analysis.

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RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

----- PREGSTAT=P

General Linear Models Procedure

Dependent Variable: T3

Pr > F	Source	DF	Sum of Squares	Mean Square	F Value
0.2451	Model	5	11145.20165145	2229.04033029	1.36
	Error	134	220332.16360855	1644.26987768	
	Corrected Total	139	231477.36526000		
T3 Mean			R-Square	C.V.	Root MSE
126.82100000			0.048148	31.97388	40.54959775

Pr > F	Source	DF	Type I SS	Mean Square	F Value
0.2451	TRT	5	11145.20165145	2229.04033029	1.36

Pr > F	Source	DF	Type III SS	Mean Square	F Value
0.2451	TRT	5	11145.20165145	2229.04033029	1.36

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November 2, 1998 23

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA
PROC GLM WITH TUKEYS

12:26 Monday,

PREGSTAT=P

General Linear Models Procedure

Dependent Variable: T4

	Source	DF	Sum of Squares	Mean Square	F Value
Pr > F					
0.0001	Model	5	12.78142465	2.55628493	5.44
	Error	134	62.99490392	0.47011122	
	Corrected Total	139	75.77632857		
T4 Mean			R-Square	C.V.	Root MSE
1.59928571			0.168673	42.87205	0.68564657

	Source	DF	Type I SS	Mean Square	F Value
Pr > F					
0.0001	TRT	5	12.78142465	2.55628493	5.44
Pr > F	Source	DF	Type III SS	Mean Square	F Value
0.0001	TRT	5	12.78142465	2.55628493	5.44

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RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA
PROC GLM WITH TUKEYS

12:26 Monday,

PREGSTAT=P

General Linear Models Procedure

Dependent Variable: TSH

	Source	DF	Sum of Squares	Mean Square	F Value
Pr > F					
0.4429	Model	5	0.46817832	0.09363566	0.96
	Error	134	13.02779597	0.09722236	
	Corrected Total	139	13.49597429		
TSH Mean			R-Square	C.V.	Root MSE
2.03757143			0.034690	15.30278	0.31180500

	Source	DF	Type I SS	Mean Square	F Value
Pr > F					
0.4429	TRT	5	0.46817832	0.09363566	0.96
Pr > F	Source	DF	Type III SS	Mean Square	F Value
0.4429	TRT	5	0.46817832	0.09363566	0.96

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November 2, 1998 25

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

----- PREGSTAT=P

General Linear Models Procedure

Duncan's Multiple Range Test for variable: T3

NOTE: This test controls the type I comparisonwise error rate, not the experimentwise error rate

Alpha= 0.05 df= 134 MSE= 1644.27

WARNING: Cell sizes are not equal.

Harmonic Mean of cell sizes= 23.30902

Number of Means	2	3	4	5	6
Critical Range	23.49	24.73	25.55	26.15	26.62

Means with the same letter are not significantly different.

Duncan Grouping		Mean	N	TRT
	A	138.93	22	1-----Control
	A			
B	A	134.31	24	2-0.1mg/kg/day
B	A			
B	A	127.61	24	4--10mg/kg/day
B	A			
B	A	126.28	23	6-100mg/kg/day
B	A			
B	A	123.89	24	5--30mg/kg/day
B				
B		110.21	23	3-1.0mg/kg/day

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RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

PREGSTAT=P

General Linear Models Procedure

Duncan's Multiple Range Test for variable: T4

NOTE: This test controls the type I comparisonwise error rate, not the
experimentwise error rate

Alpha= 0.05 df= 134 MSE= 0.470111

WARNING: Cell sizes are not equal.

Harmonic Mean of cell sizes= 23.30902

Number of Means	2	3	4	5	6
Critical Range	.3972	.4181	.4320	.4422	.4501

Means with the same letter are not significantly different.

Duncan Grouping	Mean	N	TRT
A	2.0721	24	2-0.1mg/kg/day
A	1.9191	22	1-----Control
B	1.5179	24	4--10mg/kg/day
B	1.4730	23	3-1.0mg/kg/day
B	1.4350	24	5--30mg/kg/day
B	1.1826	23	6-100mg/kg/day

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November 2, 1998 27

RABBIT DEVELOPMENTAL DATA THYROID HORMONE DATA

12:26 Monday,

PROC GLM WITH TUKEYS

----- PREGSTAT=P

General Linear Models Procedure

Duncan's Multiple Range Test for variable: TSH

NOTE: This test controls the type I comparisonwise error rate, not the
experimentwise error rate

Alpha= 0.05 df= 134 MSE= 0.097222
WARNING: Cell sizes are not equal.
Harmonic Mean of cell sizes= 23.30902

Number of Means	2	3	4	5	6
Critical Range	.1806	.1901	.1964	.2011	.2047

Means with the same letter are not significantly different.

Duncan Grouping	Mean	N	TRT
A	2.11273	22	1-----Control
A	2.09304	23	6-100mg/kg/day
A	2.05261	23	3-1.0mg/kg/day
A	2.03583	24	2-0.1mg/kg/day
A	2.00250	24	4--10mg/kg/day
A	1.93792	24	5--30mg/kg/day